

WHAT IS CLAIMED IS:

1. A molecule that specifically binds CR1, said molecule comprising amino acids sequence as described by SEQ ID NO: 2, but with one or more of the following amino acid substitutions in SEQ ID NO: 2:

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Position 17: Ser → Thr;

Position 25: Thr → Ser;

Position 29: Ile → Met;

Position 44: Asn → Lys;

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Position 45: Lys → Gly;

Position 49: Met → Ile;

Position 59: Ser → Thr;

Position 64: Leu → Val;

Position 69: Ser → Thr;

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Position 71: Thr → Ser;

Position 83: Leu → Met;

Position 111: Val → Tyr; and

Position 114: Ala → Gln.

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2. The molecule of claim 1 that has the following amino acid substitutions in SEQ ID NO: 2:

Position 17: Ser → Thr;

Position 25: Thr → Ser;

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Position 29: Ile → Met;

Position 44: Asn → Lys;

Position 45: Lys → Gly;

Position 49: Met → Ile;

Position 59: Ser → Thr;

30

Position 64: Leu → Val;

Position 69: Ser → Thr;

Position 71: Thr → Ser;

Position 83: Leu → Met;

Position 111: Val → Tyr; and

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Position 114: Ala → Gln.

3. The molecule of claim 1 that has the following amino acid substitutions in SEQ ID NO: 2:

5 Position 17: Ser → Thr;
 Position 25: Thr → Ser;
 Position 29: Ile → Met;
 Position 44: Asn → Lys;
 Position 45: Lys → Gly;
 Position 49: Met → Ile;
10 Position 64: Leu → Val;
 Position 69: Ser → Thr;
 Position 71: Thr → Ser;
 Position 83: Leu → Met; and
 Position 114: Ala → Gln.
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4. The molecule of claim 1 that has the following amino acid substitutions in SEQ ID NO: 2:

20 Position 17: Ser → Thr;
 Position 25: Thr → Ser;
 Position 29: Ile → Met;
 Position 44: Asn → Lys;
 Position 45: Lys → Gly;
25 Position 49: Met → Ile;
 Position 71: Thr → Ser;
 Position 83: Leu → Met; and
 Position 114: Ala → Gln.

30 5. The molecule of claim 1 that has the following amino acid substitutions in SEQ ID NO: 2:

 Position 17: Ser → Thr;
 Position 25: Thr → Ser;
35 Position 44: Asn → Lys;
 Position 45: Lys → Gly;
 Position 49: Met → Ile;

Position 71: Thr → Ser;
Position 83: Leu → Met; and
Position 114: Ala → Gln.

- 5 6. The molecule of claim 1 that has the following amino acid substitutions in SEQ ID NO: 2:

Position 17: Ser → Thr;
Position 44: Asn → Lys;
10 Position 45: Lys → Gly;
Position 71: Thr → Ser;
Position 83: Leu → Met; and
Position 114: Ala → Gln.

- 15 7. A molecule that specifically binds CR1, said molecule comprising an immunoglobulin variable region comprising a complementarity determining region 2 having an amino acid sequences as described by amino acid numbers 51-66 in SEQ ID NO: 2 but with one or more of the following amino acid substitutions:

20 Position 59: Ser → Thr; and
Position 64: Leu → Val.

8. A molecule that specifically binds CR1, said molecule comprising an immunoglobulin variable region comprising a complementarity determining region 3 having
25 an amino acid sequences as described by amino acid numbers 99-112 of SEQ ID NO: 2, but with the following amino acid substitution in SEQ ID NO: 2:

Position 111: Val → Tyr.

- 30 9. A molecule that specifically binds CR1, said molecule comprising an immunoglobulin variable region comprising:

(a) a complementarity determining region 1 as described by amino acid numbers 31-36 of SEQ ID NO: 2;

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- (b) a complementarity determining region 2 as described by amino acid numbers 51-66 of SEQ ID NO: 2, but with one or more of the following amino acid substitutions:

5 Position 59: Ser → Thr, and
 Position 64: Leu → Val; and

- (c) a complementarity determining region 3 as described by amino acid numbers 99-112 of SEQ ID NO: 2, but with the following amino acid substitution:

10 Position 111: Val → Tyr.

10. The molecule of any of claims 1 - 6, further comprising amino acids sequence as described by SEQ ID NO: 4, but with one or more of the following amino acid substitutions:

15 Position 15: Leu → Val;
 Position 53: Lys → Tyr;
 Position 80: His → Ser;
 Position 104: Gly → Pro;
20 Position 107: Thr → Lys;
 Position 108: Leu → Val; and
 Position 111: Arg → Lys.

25 11. The molecule of claim 10 that has the following amino acid substitutions in SEQ ID NO: 4:

 Position 15: Leu → Val;
 Position 53: Lys → Tyr;
30 Position 80: His → Ser;
 Position 104: Gly → Pro;
 Position 107: Thr → Lys;
 Position 108: Leu → Val; and
 Position 111: Arg → Lys.

35 12. The molecule of claim 10 that has the following amino acid substitutions in SEQ ID NO: 4:

Position 15: Leu → Val;
Position 80: His → Ser;
Position 104: Gly → Pro;
5 Position 108: Leu → Val; and
Position 111: Arg → Lys.

13. The molecule of claim 10 that is an immunoglobulin.

10 14. The molecule of claim 10 that is an scFv.

15. The molecule of claim 10 that is humanized.

16. The molecule of claim 10 that is chimeric.

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17. The molecule of claim 13 that is purified.

18. A hybridoma expressing the molecule of claim 13.

20 19. A molecule comprising:

(a) a first binding portion that specifically binds pathogenic antigenic molecule
desired to be reduced in amount in the circulatory system of a mammal; and

25 (b) a second binding portion that specifically binds CR1, said second binding
portion comprising an amino acid sequence as described by SEQ ID NO: 2, but with one or
more of the following amino acid substitutions in SEQ ID NO: 2:

Position 17: Ser → Thr;
30 Position 25: Thr → Ser;
Position 29: Ile → Met;
Position 44: Asn → Lys;
Position 45: Lys → Gly;
Position 49: Met → Ile;
35 Position 59: Ser → Thr;
Position 64: Leu → Val;
Position 69: Ser → Thr;

Position 71: Thr → Ser;
Position 83: Leu → Met;
Position 111: Val → Tyr; and
Position 114: Ala → Gln.

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20. The molecule of claim 19 that has the following amino acid substitutions in SEQ ID NO: 2:

Position 17: Ser → Thr;
Position 25: Thr → Ser;
10 Position 29: Ile → Met;
Position 44: Asn → Lys;
Position 45: Lys → Gly;
Position 49: Met → Ile;
Position 59: Ser → Thr;
15 Position 64: Leu → Val;
Position 69: Ser → Thr;
Position 71: Thr → Ser;
Position 83: Leu → Met;
Position 111: Val → Tyr; and
20 Position 114: Ala → Gln.

21. The molecule of claim 19 that has the following amino acid substitutions in SEQ ID NO: 2:

25 Position 17: Ser → Thr;
Position 25: Thr → Ser;
Position 29: Ile → Met;
Position 44: Asn → Lys;
Position 45: Lys → Gly;
30 Position 49: Met → Ile;
Position 64: Leu → Val;
Position 69: Ser → Thr;
Position 71: Thr → Ser;
Position 83: Leu → Met; and
35 Position 114: Ala → Gln.

22. The molecule of claim 19 that has the following amino acid substitutions in SEQ ID NO: 2:

5 Position 17: Ser → Thr;
 Position 25: Thr → Ser;
 Position 29: Ile → Met;
 Position 44: Asn → Lys;
 Position 45: Lys → Gly;
 Position 49: Met → Ile;
10 Position 71: Thr → Ser;
 Position 83: Leu → Met; and
 Position 114: Ala → Gln.

23. The molecule of claim 19 that has the following amino acid substitutions in SEQ ID NO: 2:

 Position 17: Ser → Thr;
 Position 25: Thr → Ser;
 Position 44: Asn → Lys;
20 Position 45: Lys → Gly;
 Position 49: Met → Ile;
 Position 71: Thr → Ser;
 Position 83: Leu → Met; and
 Position 114: Ala → Gln.

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24. The molecule of claim 19 that has the following amino acid substitutions in SEQ ID NO: 2:

30 Position 17: Ser → Thr;
 Position 44: Asn → Lys;
 Position 45: Lys → Gly;
 Position 71: Thr → Ser;
 Position 83: Leu → Met; and
 Position 114: Ala → Gln.

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25. The molecule of any of claims 19-24, wherein said second binding portion further comprises amino acid sequence as described by SEQ ID NO: 4, but with one or more of the following amino acid substitutions in SEQ ID NO: 4:

- 5 Position 15: Leu → Val;
 Position 53: Lys → Tyr;
 Position 80: His → Ser;
 Position 104: Gly → Pro;
 Position 107: Thr → Lys;
10 Position 108: Leu → Val; and
 Position 111: Arg → Lys.

26. The molecule of claim 25 that has the following amino acid substitutions in SEQ ID NO: 4:

- 15 Position 15: Leu → Val;
 Position 53: Lys → Tyr;
 Position 80: His → Ser;
 Position 104: Gly → Pro;
20 Position 107: Thr → Lys;
 Position 108: Leu → Val; and
 Position 111: Arg → Lys.

27. The molecule of claim 25 that has the following amino acid substitutions in
25 SEQ ID NO: 4:

- Position 15: Leu → Val;
 Position 80: His → Ser;
 Position 104: Gly → Pro;
30 Position 108: Leu → Val; and
 Position 111: Arg → Lys.

28. The molecule of claim 19, wherein said second binding portion is an immunoglobulin or an Fab region thereof.

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29. The molecule of claim 28, wherein said first binding portion is an immunoglobulin or an Fab region thereof.

30. The molecule of claim 29, wherein said first and second binding portions are cross-linked to each other.

5 31. The molecule of claim 19 that is humanized.

32. The molecule of claim 19 that is chimeric.

33. The molecule of claim 19 that is purified.

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34. The molecule of claim 25, wherein said second binding portion is an immunoglobulin or an Fab region thereof.

15 35. The molecule of claim 34, wherein said first portion is an immunoglobulin or an Fab region thereof.

36. The molecule of claim 25, wherein said first and second binding portions are cross-linked to each other.

20 37. The molecule of claim 25 that is humanized.

38. The molecule of claim 25 that is chimeric.

39. The molecule of claim 25 that is purified.

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40. A molecule comprising:

(a) a first binding portion that specifically binds

(i) an antigen of a pathogen;

30 (ii) an autoantigen; or

(ii) a blood-borne protein desired to be removed from the circulatory system of a mammal; and

(b) a second binding portion that specifically binds CR1, said binding portion
35 comprising an immunoglobulin variable region comprising a complementarity determining region 2 as described by amino acid numbers 51-66 of SEQ ID NO: 2, but with one or more of the following amino acid substitutions in SEQ ID NO: 2:

Position 59: Ser → Thr; and

Position 64: Leu → Val.

5 41. The molecule of claim 40 that has the following amino acid substitutions in SEQ ID NO: 2:

Position 59: Ser → Thr; and

Position 64: Leu → Val.

10 42. The molecule of claim 40, said immunoglobulin variable region comprising a complementarity determining region 1 as described amino acid numbers 31-36 of SEQ ID NO: 2.

43. A molecule comprising:

15 (a) a first binding portion that specifically binds

(i) an antigen of a pathogen;

(ii) an autoantigen; or

(ii) a blood-borne protein desired to be removed from the circulatory system of a mammal; and

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(b) a second binding portion that specifically binds CR1, said binding portion an immunoglobulin variable region comprising a complementarity determining region 3 as described by amino acid numbers 99-112 of SEQ ID NO: 2, but with the following amino acid substitution in SEQ ID NO: 2:

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Position 111: Val → Tyr.

44. The molecule of claim 43, said immunoglobulin variable region comprising a complementarity determining region 1 as described by amino acid numbers 31-36 of SEQ ID NO: 2.

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45. The molecule of any of claims 40-44, wherein said first and second binding portions are each an immunoglobulin or an Fab region thereof.

35 46. The molecule of any of claims 40-44, wherein said first and second binding portions are cross-linked to each other.

47. The molecule of any of claims 40-43 that is humanized.

48. The molecule of any of claims 40-43 that is chimeric.

5 49. The molecule of any of claims 40-43 that is purified.

50. The molecule of claim 19 that is a dimeric molecule comprising a first polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and
10 wherein the first polypeptide and the second polypeptide is each independently selected from the group consisting of (a) a third polypeptide consisting essentially of, in amino- to carboxy-terminal order, an immunoglobulin variable light chain domain, an immunoglobulin constant light chain domain, a linker polypeptide, an immunoglobulin variable heavy chain domain, a CH1 domain, an immunoglobulin hinge region, a CH2 domain, and a CH3
15 domain; and (b) a fourth polypeptide consisting essentially of, in amino- to carboxy-terminal order, a scFv, a CH1 domain, an immunoglobulin hinge region, a CH2 domain, and a CH3 domain.

51. The molecule of claim 25 that is a dimeric molecule comprising a first
20 polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and wherein the first polypeptide and the second polypeptide is each independently selected from the group consisting of (a) a third polypeptide consisting essentially of, in amino- to carboxy-terminal order, an immunoglobulin variable light chain domain, an immunoglobulin
25 constant light chain domain, a linker polypeptide, an immunoglobulin variable heavy chain domain, a CH1 domain, an immunoglobulin hinge region, a CH2 domain, and a CH3 domain; and (b) a fourth polypeptide consisting essentially of, in amino- to carboxy-terminal order, a scFv, a CH1 domain, an immunoglobulin hinge region, a CH2 domain, and a CH3 domain.

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52. The molecule of claim 19 that is a polypeptide, said polypeptide consisting essentially of, in amino- to carboxy-terminal order, a first polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and wherein the first polypeptide
35 consists essentially of, in amino- to carboxy-terminal order, a first scFv, a CH2 domain, and a CH3 domain; and the second polypeptide consists essentially of, in amino- to carboxy-terminal order, a second scFv domain.

53. The molecule of claim 25 that is a polypeptide, said polypeptide consisting essentially of, in amino- to carboxy-terminal order, a first polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and wherein the first polypeptide consists essentially of, in amino- to carboxy-terminal order, a first scFv, a CH2 domain, and a CH3 domain; and the second polypeptide consists essentially of, in amino- to carboxy-terminal order, a second scFv domain.

54. The molecule of claim 19 that is a polypeptide, said polypeptide consisting essentially of, in amino- to carboxy-terminal order, a first polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and wherein the first polypeptide consists essentially of, in amino- to carboxy-terminal order, a first scFv, a CH3 domain, and a CH2 domain; and the second polypeptide consists essentially of, in amino- to carboxy-terminal order, a second scFv domain.

55. The molecule of claim 25 that is a polypeptide, said polypeptide consisting essentially of, in amino- to carboxy-terminal order, a first polypeptide and a second polypeptide, wherein the first polypeptide comprises the first binding domain and the second polypeptide comprises the second binding domain, and wherein the first polypeptide consists essentially of, in amino- to carboxy-terminal order, a first immunoglobulin variable heavy chain, a first immunoglobulin variable light chain, a CH2 domain and a CH3 domain; and the second polypeptide consists essentially of, in amino- to carboxy-terminal order, a second immunoglobulin variable heavy chain, and a second immunoglobulin variable light chain.

56. The molecule of any of claims 50-55, wherein said first and second binding domains are each an immunoglobulin or an Fab region thereof.

57. A method for removing a blood-borne antigen, autoantigen or pathogen from the circulation of a mammal comprising administering to said mammal an amount of the molecule of claim 25, effective to remove the antigen of interest from the circulation of the mammal.

58. The method of claim 57, wherein said mammal is a human.

59. A method for removing a blood-borne antigen, autoantigen or pathogen from the circulation of a mammal, wherein the antigen, autoantigen or pathogen is expressed in the circulation of said mammal, said method comprising administering to said mammal an amount of the molecule of claim 25, effective to remove the antigen of interest from the
5 circulation of the mammal.

60. The method of claim 59, wherein said mammal is a human.

61. A pharmaceutical composition comprising a therapeutically effective amount of
10 the molecule of claim 25; and a pharmaceutically acceptable carrier.

62. A kit comprising in one or more containers, one or more isolated nucleic acids encoding the molecule of claim 25.

15 63. A kit comprising in one or more contained a cell transformed with one or more nucleic acids encoding molecule of of claim 25.